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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,532	10/19/2001	Soren Michael Madsen	54320.000010	8165

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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/982,532	MADSEN ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *12-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6* is/are rejected.

7)☒ Claim(s) *4,5 and 7-11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I (Claims 1-11) in the paper filed July 9, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-29 are pending in the instant application. Claims 12-29 are withdrawn as being drawn to a non-elected invention. Claims 1-11 are under examination in the instant application.

Priority

Applicant's claim for domestic priority to US Application 09/692,204 under 35 U.S.C. 120 is acknowledged.

Information Disclosure Statement

The information disclosure statement filed January 29, 2002 has been considered, and a signed and initialed copy of the form PTO-1449 is attached to this Office Action.

Specification

The disclosure is objected to because of the following informalities: Figure 1 has panels A and B, but there is no clearly indicated description of Figure A, although there is a clear description of Figure B. It would be remedial to insert the term "Fig. 1A" in the appropriate position in the description.

Appropriate correction is required.

Claim Objections

Claims 4 and 5 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must be multiply dependent in the alternative form. See MPEP § 608.01(n). In the instant case, Claim 4 (and 5, by its dependency) is dependent on claim 1 (by virtue of its recitation in the preamble of the claim) *and* claim 2 (by virtue of its recitation in the body of the claim), simultaneously (i.e., not in the alternative). Accordingly, claims 4 and 5 have not been further treated on the merits.

Claims 8-11 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot be dependent on a multiple dependent claim. See MPEP § 608.01(n). In the instant case, claims 7 and 8 depend from claim 6, which is multiply dependent on claims 1 or 2. Accordingly, claims 7-11 have not been further treated on the merits.

Claim 2 is objected to because of the following informalities: claim 2 refers to Table 2 in the body of the claim, which is generally improper. It would be remedial to indicate SEQ ID NO: 4 in place of Table 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a polynucleotide encoding a protein that is at least 15% identical to OrfY protein, or a fragment thereof, wherein the protein or fragment thereof has at least partial promoter regulatory activity. The claims read on a broad genus of proteins and fragments that must necessarily have the promoter regulating activity.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims a polynucleotide encoding a protein that is at least 15% identical to OrfY protein (or a fragment thereof) by function only, without any disclosed or known correlation between the elements and their function. The specification only provides teachings regarding a single polynucleotide (SEQ ID NO: 3) encoding a single OrfY protein (SEQ ID NO: 4), wherein said protein has promoter regulatory activity. The specification does not teach what fragments or domains of the OrfY protein are necessary or sufficient to convey the promoter

regulatory activity. As such, the skilled artisan cannot envision what 85% of the protein can be changed while retaining the necessary biological activity, nor can the skilled artisan envision which fragments of the protein (either 100% identical to SEQ ID NO: 4, or otherwise) also retain the required biological activity. Because the skilled artisan cannot envision which proteins necessarily have this activity, the skilled artisan also cannot envision which polynucleotides would encode such proteins.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that allows one to envision a representative number of polynucleotides encoding a protein that is at least 15% identical to OrfY protein, or a fragment thereof, wherein the protein of fragment thereof has at least partial promoter regulatory activity, by disclosing structural or functional features of the OrfY protein so that one of skill in the art could envision the corresponding polynucleotides of the claimed invention. Indeed, the prediction of function based on sequence homology has been shown in the prior art to have numerous deficiencies. This was demonstrated by the conflicting publications of Scott *et al.* (*Nature Genetics* **21**: 440-443, 1999; see entire document; henceforth Scott) and Everett *et al.* (*Nature Genetics* **17**: 411-422, 1997; see entire document; henceforth Everett) regarding the cloning and characterization of PDS. Everett initially identified and sequenced the protein, predicting based upon the sequence that the PDS gene product functioned as a sulphate ion transporter protein because of its similarity to a family of known sulphate ion transporters (see for example the Abstract and page 419, right column, second full paragraph). However, further characterization done by Scott indicated that PDS was not a sulphate ion transporter because it was unable to transport sulphate ions; rather, Scott identified that PDS was

a chloride and iodide ion transporter (see for example the Abstract and page 440, the paragraph bridging the left and right columns to the second full paragraph). Scott further indicated that their results underscored the importance of establishing function even in the face of significant homology to proteins of known function (see for example page 441, left column, third full paragraph), thereby establishing that function based on homology is an unpredictable endeavor. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

The instant claims read on polynucleotides encoding a protein with as little as 15% identity to the only protein described in the specification, as well as fragments of the protein. The claims require that the protein variant or fragment thereof maintain the biological activity of the single full-length protein that is described in the specification, OrfY (SEQ ID NO: 4). Thus, in order to envision a polynucleotide that encodes a fragment or variant of the OrfY protein, there must be some structure-function relationship that indicates what portions of the protein are required for its function. However, the specification does not describe such a structure-function relationship, and the prior art does not remedy this deficiency. Indeed, the prior art indicates that predicting function based on homology alone is not sufficient to allow one of skill in the art to envision the claimed invention. As such, the instant specification does not describe the claimed invention of any polynucleotide that encodes a protein having 15% identity to OrfY, or a fragment of the protein (or a 15% identical variant, etc.), wherein the protein maintains its promoter regulatory activity. Therefore, the Written Description of the claimed invention is not satisfied.

Claims 1-3, 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), and the most relevant factors are indicated below:

Nature of the invention. The nature of the invention is a polynucleotide that encodes an OrfY protein that must necessarily have a promoter regulatory activity. The instant specification describes a single OrfY protein with a promoter regulatory activity, identified as SEQ ID NO: 4. The claimed polynucleotide is claimed to have as little as 15% identity to the OrfY protein described in the specification (SEQ ID NO: 4), or be any fragment of either the 100% identity OrfY or 15% identical OrfY protein (or any % identity in between).

It is noted that the disclosed OrfY protein (SEQ ID NO: 4) contains 227 amino acids. Thus, a protein with as little as 15% identity to SEQ ID NO: 4 can have as many as 193 amino acid changes, which is effectively an entirely different protein. Taking into consideration the fact that a polynucleotide encoding any fragment of a protein with as much as 193 amino acids

changed is also claimed, the invention reads on any 193 (or fewer) amino acid protein that has a promoter regulatory activity. Thus, the nature of the invention is effectively a polynucleotide encoding any protein having promoter activity. As such, in order for the claims to be enabled, one of skill in the art would need to make any protein having as little as 15% identity to SEQ ID NO: 4 (or fragment of said protein) that necessarily had a promoter regulatory activity

Scope of the invention. The scope of the invention is very broad. It encompasses any 193 (or fewer) amino acid protein with promoter regulatory activity (see above). It also encompasses a vast number of polynucleotides encoding proteins with as little as 15% identity to the only disclosed embodiment of the invention, with no guidance as to what 85% of the protein can be changed while retaining a promoter regulatory activity.

State of the art and Level of skill in the art. The state of the art is silent with regard to the specific domains within OrfY that confer a promoter regulatory activity. As a result one of skill in the art could not consult the art in terms of making a polynucleotide that encoded a 15% identical variant or fragment of the OrfY protein that necessarily had a promoter regulatory activity.

Furthermore, as indicated above in the rejection under Written Description, the prediction of function based on sequence homology is an unpredictable art. This was demonstrated by the conflicting publications of Scott *et al.* (*Nature Genetics* **21**: 440-443, 1999; see entire document; henceforth Scott) and Everett *et al.* (*Nature Genetics* **17**: 411-422, 1997; see entire document; henceforth Everett) regarding the cloning and characterization of PDS. Everett initially identified and sequenced the protein, predicting based upon the sequence that the PDS gene product functioned as a sulphate ion transporter protein because of its similarity to a family of

known sulphate ion transporters (see for example the Abstract and page 419, right column, second full paragraph). However, further characterization done by Scott indicated that PDS was not a sulphate ion transporter because it was unable to transport sulphate ions; rather, Scott identified that PDS was a chloride and iodide ion transporter (see for example the Abstract and page 440, the paragraph bridging the left and right columns to the second full paragraph). Scott further indicated that their results underscored the importance of establishing function even in the face of significant homology to proteins of known function (see for example page 441, left column, third full paragraph), thereby establishing that function based on homology is an unpredictable endeavor. This is exemplified by US 6,583,275, which teaches a polynucleotide (SEQ ID NO: 4963) encoding a protein fragment having 31.2% homology to SEQ ID NO: 4. Although this meets the limitations with regard to the structural requirements of the claims, one cannot predict whether the protein has the required functional activity based simply on homology alone.

In the absence of specific guidance in the prior art with regard to the OrfY protein and its functional domains, and in view of the unpredictability concerning predicting structure based on homology alone, the skilled artisan would be required to consult the specification on how to make a polynucleotide encoding a protein that is at least 15% identical to OrfY protein (or a fragment thereof), wherein the protein of fragment thereof has at least partial promoter regulatory activity.

Number of working examples and Guidance provided by applicant. The instant specification refers to a single example of an OrfY protein that has a promoter regulatory activity (SEQ ID NO: 4). As such, the skilled artisan would only be apprised as to how to make a

polynucleotide encoding that particular OrfY protein. This is because there is no further guidance in the specification regarding a structure-function relationship for the OrfY protein and the required promoter regulatory activity. In the absence of a teaching as to what domains are specifically required for the promoter regulatory activity of an OrfY protein, the skilled artisan could not routinely make a protein with as little as 15% identity to SEQ ID NO: 4 which retains the promoter regulatory activity. Similarly, the skilled artisan would be unable to make fragments of SEQ ID NO: 4 (or a protein with 15% identity to SEQ ID NO: 4) that necessarily had the activity.

Unpredictability of the art and Amount of experimentation required. The claimed invention is vastly unpredictable. The invention reads on a polynucleotide encoding any 193 (or fewer) amino acid protein with promoter regulatory activity, but the specification provides no guidance on how to make any of these protein or their respective polynucleotides. Furthermore, the claims read on polynucleotides encoding any protein having 15% identity to SEQ ID NO: 4, but the specification provides no guidance with regard to what 85% of the protein can be altered without changing the function of the protein. As a result, the skilled artisan would have to empirically determine which domains of the OrfY protein were required for its promoter regulatory activity, as well as determine which 193 (or fewer) amino acid proteins had promoter regulatory activity. This represents an undue amount of unpredictable trial and error experimentation because the skilled artisan has no way to predict which proteins or fragments will have the required functional activity. As a result, the claimed invention is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "OrfY as defined herein" in the body of the specification. It is unclear what "herein" refers to (i.e., the specification, in the claims below, etc.). Additionally, it is unclear what parameters, set forth "herein," are to be considered as limitations in the claims. There is no clear definition as to what an "OrfY" comprises by indicating the term in parenthesis, and defining the term. It would be remedial to indicate a SEQ ID NO next to the term "OrfY" in order to distinctly define what the term is meant to encompass.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

In the interest of compact prosecution, the Office is interpreting the indefinite term "OrfY described herein" as being indicative of SEQ ID NO: 4, and the polynucleotide sequence (SEQ ID NO: 3) encoding SEQ ID NO: 4.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,583,275 (see entire document; henceforth the '275 patent).

The '275 patent teaches the polynucleotide SEQ ID NO: 4963, which encodes a polypeptide fragment that is 31.2% identical to SEQ ID NO: 4 of the instant application. Because SEQ ID NO: 4963 comprises the necessary structural features set forth in the claims, it inherently possesses the promoter regulatory activity set forth in the claims, absent evidence to the contrary. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). As such, the '275 patent anticipates the claimed invention.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
AU 1636

JAMES KETTER
PRIMARY EXAMINER